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PATENT
Our Docket: 931800

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

WAYNE A. BORDER
ERKKI I. RUOSLAHTI

Serial No.: 07/416,656

Filed: October 3, 1989

For: INHIBITING TRANSFORMING GROWTH FACTOR ß TO PREVENT ACCUMULATION OF EXTRACELLULAR MATRIX

Group Art Unit: 1806

Examiner: S. Ziska

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 3/19/92
Date

By Theresa A. Brown
Theresa A. Brown, Reg. No. 32,547

3/19/92
Date of Signature

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

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INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37.C.F.R. § 1.97, enclosed are references relating to the above-identified application, which is a continuation-in-part of U.S. Serial No. 07/415,081, filed September 29, 1989. For the convenience of the Examiner, these references are listed on the attached Form PTO-1449 and a copy of each is enclosed herewith. Also attached is a copy of the Search Report issued in the related PCT Application No. PCT/US90/05566.

The present application is directed to a method treating pathologies characterized by an accumulation of extracellular matrix components by suppressing the activity of TGFß. The claimed invention is also useful for diagnosing such pathologies by determining the level of TGFß in the tissues.

The provided references are relevant for the general disclosure of TGFß, as it relates to extracellular matrix

proteins. However, these references, whether considered individually or in combination, neither anticipate nor render obvious the claimed invention.

WO 88/03151 was cited in the Search Report of the PCT application related to the present application. Page 31, line 15 through page 32, line 8 was specifically cited as the relevant portion of this document. The reference, however, is directed to polypeptides that selectively inhibit or promote thrombin-mediated mitogenesis and not the control of TGFß activity.

Ignotz and Massague (1986) report that TGFß increases the expression of fibronectin and collagen in various cells in culture, and the incorporation of fibronectin and collagen into the extracellular matrix. Ignotz and Massague further report that the anchorage-independent growth of fibroblasts by TGFß can be mimicked with fibronectin and can be blocked by inhibitors of fibronectin binding to the fibronectin receptor.

Roberts et al. (1986) report that injection of TGFß, but not EGF or PDGF, into newborn mice induces angiogenesis and collagen formation. The induction of collagen formation in response to TGFß can be inhibited by antibodies specific for TGFß.

Bassols and Massague (1988) describe the induction of proteoglycan gene expression by TGFß. Bassols and Massague further report that TGFß controls chain elongation and termination during biosynthesis of proteoglycans.

Border et al. (1988) describe the induction of proteoglycans in mesangial cells in response to TGFß, suggesting TGFß may have a role in the production of glomerulonephritis.

Flanders et al. (1988) describe antibodies reactive for TGFß and the use of the antibodies, for example, to detect the presence of TGFß in a sample or to block the binding of TGFß to the TGFß receptor.

MacKay et al. (1989) report the presence of TGFß receptors on glomerular epithelial, endothelial and mesangial cells. MacKay et al. describe effect of TGFß on the proliferation of glomerular cells in cell culture and on the production of collagen and fibronectin by glomerular cells.

Connor et al. (1989) report that the degree of intraocular fibrosis following retinal surgery is correlated to the level of TGFß. The activity was primarily due to TGFß2, although some activity was also due to TGFß1.

Chen et al. (1987) describe the stimulatory effect of TGF-ß on the synthesis of at least two types of chondroitin sulfate proteoglycans in nonproliferating human arterial smooth muscle cells in culture. The authors also report that TGF-ß neither significantly stimulated proliferation of quiescent smooth muscle cells nor inhibited proliferating cells. TGF-ß was found not to have a comparable stimulating effect on endothelial cell proteoglycan synthesis as it did on arterial cells.

It is respectfully requested that these references be considered in the examination of this application and that their consideration be made of written record in the application file.

Respectfully submitted,

3/19/92
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